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Original Article

Does Improvement in Respiratory Function after Hemodialysis Correlate with Ultrafiltration Volume?

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ABSTRACT

Objectives: To evaluate the effect of mechanical ultrafiltration on improvement in respiratory functions among patients of end-stage renal disease dependent on hemodialysis.
Study design: Cross-sectional analytical study.
Place and Duration of Study: Dialysis Unit, Combined Military Hospital Peshawar, Pakistan, from Sep to Nov 2021
Methodology: Patients on maintenance hemodialysis for at least three months were included. Patients with altered mental status and gross rheumatological abnormalities and unwilling patients were excluded. Spirometry was done before and after mid-week dialysis sessions thrice at two minutes intervals and the best values recorded. Different spirometry parameters before and after dialysis session were compared. The relationship of changes in these parameters with ultrafiltration volumes was also examined.
Results: A total of 50 patients were enrolled of which 36(72%) were females and 14(28%) were males. The mean age was 48.76±11.72 years. Low and high ultrafiltration groups included 26 and 24 patients, respectively. The median ultrafiltration volume was 1.5(1.00-2.80) liters. The majority of the patients showed restrictive pattern. The mean FEV1 percentage was 48.87±17.35 and 57.94±75.34 before and after hemodialysis respectively (p=0.387). The mean FVC percentage was 50.62±19.28 and 46.04±18.73 before and after the hemodialysis respectively (p=0.056). FEV1/FVC percentage was significantly different before and after hemodialysis i.e.106.7±24.0 and 113.30±16.94, respectively (p=0.014).
Conclusion: Lung parameters improved slightly in patients after dialysis. However, ultrafiltration volume did not have significant change on any of the measured parameters.

Keywords: Hemodialysis, Spirometry, Ultrafiltration volume.

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INTRODUCTION

End-stage renal disease (ESRD) is a major health problem across the world and is associated with considerable morbidity and mortality.[1] ESRD results in dependency on renal replacement therapy in the form of hemodialysis (HD). Changes in body fluid status and inter-dialytic weight gain are common in these patients because of oliguria/ anuria.[2] Systemic manifestations are also a part of this disease. Respiratory system integrity and function are frequently affected in such patients on long-term dialysis. Patients could thus develop pulmonary edema due to increased capillary permeability, pleural effusions, calcified lesion in the lungs, fibrosis, hypoxemia, and restrictive type of changes on lung function assessment in majority.[3-6] In a study carried out by Yilmaz *et al*., on Turkish patients with ESRD, it was concluded that fluid overload is closely associated with restrictive and obstructive respiratory abnormalities.[7] They concluded that HD had a beneficial effect on pulmonary function tests, which may be due to the reduction of volume overload. In another study on pulmonary functions among ESRD patients, Sharma and associates found that the majority of their patients had restrictive and mixed respiratory disorders, and pulmonary function tests significantly improved after HD; however, normal predicted values were still not achieved.[8] It is expected that HD can lead to improvement in pulmonary functions as it removes excess body fluid and toxins due to raised urea levels. In Pakistan, restrictive spirometry patterns have been reported among ESRD patients by Anees *et al*., though they did not find any improvement in pulmonary functions.[9] Local data on this aspect is still scarce, especially from Khyber Pakhtunkhwa. We, therefore, planned this study to find out the effect of HD on dynamic lung volumes and its relation with ultra-filtration volume in patients

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with ESRD. The results could help us in emphasizing the importance of fluid restriction while counselling the patients about treatment modalities for ESRD other than HD.

METHODOLOGY

This cross-sectional analytical study was conducted in the Dialysis Unit of Combined Military Hospital, Peshawar Pakistan from September to November 2021. Permission was obtained from the Ethics Review Committee of the hospital vide serial No. 39/21. Verbal consent was obtained from all patients before enrollment. Patients were enrolled through consecutive sampling.

Sample size calculation was done suing Epitools sample size calculator. We assumed the expected change in FVC% from 77.03±24.32 to 81.61±23.33 as quoted in the study by Yilmaz *et al.*,[7] We set the confidence interval at 95%, power at 80% and ratio of sample size 1:1 in both groups using two tailed test.

Inclusion Criteria: Patients with atleast three months of HD vintage, aged 18-70 years, and being concious and hemodynamically stable were included in the study.

Exlusoin Criteria: Patients with altered mental status, and gross rheumatological abnormalities and those who did not give consent were excluded from the study.

Baseline demographic data was recorded. HD was carried out for 3.5 hours using a standard prescription on Fresenius F4008 hemodialysis machines. Patients were ultra-filtrated to their usual dry weight. The spirometry procedure was explained to all patients before their assessment, and a practical demonstration was also given to patients who could not comprehend the verbal instructions. A total of three attempts with two minutes intervals were performed by every patient using a portable Spirolab spirometer, both before and after the HD sessions. The best among the three attempts was included in the final analysis.

Forced vital capacity (FVC), forced expiratory volume in 1st second (FEV1), FEV1/FVC% ratio, peak expiratory flow rate (PEFR), forced expiratory flow between 25-75% of the FVC (FEF25-75%), and maximum voluntary ventilation (MVV) were recorded as predicted of patient's age, height, weight, and gender. Based on standard criteria, lung functions were divided into normal, restrictive lung disorder, and obstructive lung disorder.[10]

Data were analyzed using SPSS 23.00. Continuous variables with parametric distribution were described as mean±SD, whereas those with non-parametric distribution were described as median and interquartile ranges. The normality of data was assessed using Shapiro- Wilk test. Paired samples T-test was used to compare the means of all the parameters before and after HD. Change in both the groups was analyzed by applying the independent sample T-test. For the later analysis, patients with UF volumes of up to 1.50 liters were included in the low UF group, whereas the rest were included in the high UF group. The *p*-value of <0.05 was considered significant.

RESULTS

A total of 50 patients fulfilling the inclusion criteria were enrolled in the study, out of which 36(72%) were female and 14(28%) were males. The mean age of the patients was 48.76±11.72 years. The mean duration of hemodialysis was 13±31.72 months and the median UF volume was 1.5L(1.00-2.80) (Table-I). The most common cause of ESRD was diabetic nephropathy in 25(50%) followed by hypertensive nephropathy in 15(30%), chronic glomerulonephritis in 3(6%), and nephrolithiasis in 2(4%) patients. The mean dry weight of our subjects was 59.52±14.94 kg. All the observed spirometry values in our patients were less than the predicted values of their respective demographics. The majority of the patients showed restrictive patterns (FEV1/FVC>80%). Mean FEV1 percentage was 48.87±17.35 and 57.94±75.34 before and after HD respectively (*p*=0.387). The mean FVC percentage was 50.62±19.28 and 46.04±18.73 before and after the HD respectively (*p*=0.056) (Table-II). FEV1/FVC percentage was statistically significant before and after HD and was 106.7±24.0 and 113.30±16.94 respectively (*p*=0.014) (Table-II). Low UF and high UF groups included 26(52%) and 24(48%) patients respectively. FVC and MVV showed negative correlation with UF in both the groups. However, none of the parameters showed significant change in both groups before and after HD using UF as a categorical variable. (Table-III). Linear regression analysis was performed where UF was taken as independent variable and spirometry variables were taken as dependant variables. However, we did not find any statistically significant association between these variables (Table-IV). Pre-dialysis spirometry values were compared in both groups which showed statistically significant raised FEV/FVC ratio in high

UF group (p=0.016). None of the other variables had significant difference in both groups (Table-V).

Table-I. Demographic Parameters and Duration of Hemodialysis

S. No.	Variable	Value
1	Age	48.76±11.71
2	**Gender, n(%)** Male Female	 14(28%) 36(72%)
3	Weight (kg)	59.52±14.94
4	Hemodialysis vintage (months)	13±31.72
5	UF (L)	1.50(1.00-2.80)

Table-II. Spirometry Parameters Before and After Hemodialysis

S.No.	Parameter (%)	Before HD	After HD	*p*-value
		Mean±SD		
1	FVC	50.62±19.28	46.04±18.73	0.056
2	FEV1	48.87±17.35	57.94±75.34	0.387
3	FEV1/FVC	106.7±24.0	113.30±16.94	0.014
4	PEFR	34.06±15.70	36.32±16.95	0.249
5	FEF25-75%	46.12±21.25	46.24±19.01	0.964
6	MVV	40.38±14.08	39.64±16.18	0.615

Table-III. Correlation of Different Spirometry Variables with Ultrafiltration Volume

S. No.	Parameter (%)	Low UF (n=26)	High UF (n=24)	*p*-value
1	FVC	-6.31±20.47	-2.71±10.89	0.447
2	FEV1	-1.60± 17.29	20.63±104.47	0.290
3	FEV1/FVC	10.15±23.73	2.75±8.14	0.144
4	PEFR	2.65±14.48	1.83±13.01	0.835
5	FEF25-75%	-0.46±22.45	0.75±14.66	0.821
6	MVV	-0.88±12.03	-0.58±8.37	0.918

Table-III. Correlation of Different Spirometry Variables with Ultrafiltration Volume

S. No.	Parameter (%)	Low UF (n=26)	High UF (n=24)	*p*-value
1	FVC	-6.31±20.47	-2.71±10.89	0.447
2	FEV1	-1.60± 17.29	20.63±104.47	0.290
3	FEV1/FVC	10.15±23.73	2.75±8.14	0.144
4	PEFR	2.65±14.48	1.83±13.01	0.835
5	FEF25-75%	-0.46±22.45	0.75±14.66	0.821
6	MVV	-0.88±12.03	-0.58±8.37	0.918

Table-IV. R2 and *p*-values on Linear Regression Analysis

S. No.	Parameter	R2	*p*-value
1	FVC	0.012	0.447
2	FEV1	0.023	0.290
3	FEV1/FVC	0.042	0.153
4	PEFR	0.001	0.835
5	FEF25-75%	0.001	0.824
6	MVV	0.000	0.919

Table-V. Pre-dialysis Values of all the Parameters of Patients Among Both Groups

S. No.	Parameter	Low UF	High UF	*p*-value
1	FVC	52.88±21.98	48.17±15.96	0.387
2	FEV1	47.4±18.52	50.46±16.23	0.537
3	FEV1/FVC	98.96±30.33	115.08±9.74	0.016
4	PEFR	31.15±13.60	37.21±17.45	0.181
5	FEF25-75%	44.77±21.26	47.58±21.56	0.645
6	MVV	39.00±13.48	41.88±14.83	0.478

DISCUSSION

ESRD is a major global burden and is associated with increased mortality and worse outcomes. Its incidence has been increased for the past few years and is still on the rise. In Pakistan, 21.2% of adults suffer from ESRD.[11] It affects the functions of almost every system of the body including heart, lungs, and electrolytes. It has also been found to be associated with, anemia, vascular changes, hypertension, protein-energy wasting, and inflammation, which are predictors of progression of the disease affecting other systems of the body.[12-14] Though, fluid accumulation in the lungs is a frequent cause of outpatient visits among these patients, studies on pulmonary functions in these patients has been performed infrequently. Authors from different countries have reported predominantly restrictive disorders in their subjects on spirometry with some studies showing mixed obstructive/restrictive patterns as well in these patients.[7,15,16] Pre-dialysis values of spirometry variables in our study also showed significantly raised FEV1/FVC ratio in high UF group supporting presence of restrictive pattern in this group. Female predominance (72%) was seen in our subjects with diabetic nephropathy (50%) as the most common cause. Mean age was below 50 years concerning the growing ESRD burden more in the early age group. Only five patients underwent HD with zero UF volume. We found that our patients had markedly reduced pulmonary functions as predicted by their age, height, weight, and gender. This effect may be due to overall poor effort due to muscular weakness and poor quality of life among these patients. The restrictive pattern was seen as the predominant pulmonary dysfunction in a majority of our subjects and it validates the findings presented in the studies worldwide.[8,9,16,17]

Our data showed mean FEV1 percentages of 48.87±17.35 and 57.94±75.34 before and after hemodialysis respectively. These percentages are higher than another study with same sample size performed by Sharma *et al*., however, we could not find significant relation with HD.[8] Findings reported by Anees *et al*., also did not show any significant relation of FEV1 with HD and is in accordance with our result.[9]

Mean FVC percentage was 50.62±19.28 and 46.04±18.73 before and after HD respectively. The decline in FVC in post-dialysis data shows a negative correlation of hemodialysis with FVC. Findings from the other authors showed significant FVC improvement in post-dialysis patients.[8,15,16] It also points out the concern for factors other than fluid overload in such patients responsible for abnormal results in these patients.

FEV1/FVC percentage was 106.7±24.0 initially which later on improved to 106.7±24.0 and was statistically significant. This improvement can be explained by the negative correlation of FVC leading to improved FEV1/FVC ratio. The finding is consistent with the results reported by Hasan *et al.*, derived from thirty ESRD patients.[16] Other authors we compared did not show any significant improvement in their results.[7-9,15] It may be because of the smaller sample size in all of the mentioned studies. However, this association was lost when linear regression analysis was applied (p >0.05) as shown in Table-IV.

Mean percentages of PEFR were 34.06±15.70 and 36.32±16.95 before and after hemodialysis respectively. These values are less than those reported by other authors who found significant improvement in their post-dialysis measurements.[8,16] In contrast to this, in the study conducted by Yilmaz *et al*., on 54 ESRD patients, no statistical significance was found.[7]

FEF25-75% was also lower (46.12±21.25 and 0.75±14.66) in our subjects than reported by Hasan *et al.*, and Sharma *et al*., who found significant improvement in their results.[8,16] Our finding of PEFR supports the finding reported by Yilmaz *et al*., with no significant improvement in post-dialysis patients.[7]

None of the mentioned studies compared the MVV in their subjects. Besides, this parameter also had no significant improvement in our data.

Pre-dialysis values in both groups were compared which showed significantly higher FEV1/FVC ratio in the high UF group as displayed in Table-V. This higher ratio is again due to higher FVC and lowers FEV1 in the respected group leading to an increased ratio. These changes in fluid overloaded patients need further large number of studies to evaluate the possible mechanism among these subjects. The rest of the measured values were lower in the low UF group but did not have a significant difference. Authors from another study also reported significantly lower values in patients without fluid overload.[7]

Yilmaz *et al*., conducted their research in fluid overloaded patients and found a significant negative correlation between fluid overload and spirometry variables studied.[7] Our comparison among both groups could not establish significant change among both groups. These findings are consistent with the results published by Lang *et al*., who found that there was no significant relation of fluid removal with lung parameters.[17] These findings raise the question of factors involved other than fluid overload in abnormal respiratory parameters among these patients. These may include inflammatory and toxic effects of metabolites on lung functions. It also supports the fact that acute change among these patients who are on long-term hemodialysis does not affect directly spirometry values as concluded by Lang *et al*.[17] Further large studies are needed to evaluate the role of mechanical UF in these patients. These insignificant results are may be due to skeletal muscle weakness causing restricted respiratory muscles movements among ESRD patients. This phenomenon has been explained by a study conducted in Brazil by Juliana and co-authors.[18] They concluded that respiratory muscle strength, lung function, and functional capacity in patients undergoing hemodialysis were of lower values than those of the general population.

A notable limitation of our study was that we did not group patients who had hemodialysis with no UF volume.

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CONCLUSION

Lung parameters improved slightly in patients after dialysis. However, ultrafiltration volume did not have significant change on any of the measured variable.

Conflict of Interest: None.

Disclosure

The data from this study have been presented as an oral presentation in 14thBIENNIAL CHESTCON organized by Pakistan Chest Society from 3rd to 5th December 2021.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

NS & MA: Data acquisition, critical review, approval of the final version to be published.

ARA & ZUA: Conception, study design, drafting the manuscript, approval of the final version to be published.

SZU & RI: Data analysis, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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